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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/657,383	09/08/2003	Yan Chang	104831-0002-103	9375

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MAIER, LEIGH C	
ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/657,383	CHANG ET AL.	
	Examiner	Art Unit	
	Leigh C. Maier	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-12,15-23,25,26 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-12,15-23,25,26 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/30/07, 9/28/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 18, 2007 has been entered.

Claims 1, 20-23 and 28 have been amended. Claims 13, 14, 24 and 27 have been canceled. Claims 1-5, 7-12, 15-23, 25, 26 and 28 are pending. Any objection or rejection not expressly repeated has been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. The rejections herein have been revised from the previous Office action. The arguments presented will be addressed insofar as they apply to the current rejections.

Information Disclosure Statement

It is noted that the IDS submitted October 30, 2007 is identical to the one submitted September 28, 2007. The form PTO-1449 has been marked through to indicate that it is a duplicate.

Claim Rejections - 35 USC § 112

Claims 1-3, 7, 18-22, 25 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, as set forth in the previous Office action. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that Applicant, at the time the application was filed, had possession of the claimed invention.

Applicant has asked for clarification of the new matter rejection of record in the previous Office action. This rejection has been reconsidered and revised.

Independent claim 1 recites a carbohydrate that "comprises a polymeric backbone." The examiner does not find support for a generic polymeric limitation. Page 5 of the specification discusses carbohydrate agents generally. The closest support the examiner finds is at lines 17-19: "A preferred class of therapeutic materials comprises oligomeric or polymeric species having one or more sugars such as galactose or arabinose pendant therefrom." This is consistent with the passages cited by Applicant at page 4 reciting "a polymeric backbone having side chains dependent therefrom. The side chains are terminated by a galactose or arabinose unit." Therefore, there does not appear to be support for a generic polymeric agent. The specification appears to provide support only for those having some sort of branching and further comprising a saccharide moiety that interacts with a galectin.

Claim Rejections - 35 USC § 103

Claims 1-4, 7, and 18-28 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Klyosov et al (US 6,645,946), as set forth in the previous Office action.

Klyosov '946 teaches the administration of galactomannan and 5-FU by injection to mice. See examples. It is noted that the mice in the examples do not actually have cancer. The reference also describes the structure of galactomannan. See paragraph bridging col 5-6. This structure appears to meet the criteria of carbohydrates that would bind to galectin-1 or galectin-3.

Although the reference does not exemplify administration to a patient having cancer, the reference specifically suggests the administration of the galactomannan/chemotherapeutic agent as a treatment for cancer. See col 2, lines 15-65. The reference teaches that the administration of the galactomannan reduces side effects produced by toxic chemotherapeutic agents. See abstract. The reference further suggests a variety of modes of administration, including oral, and sequential administration of the galactomannan and chemotherapeutic agent. See col 3, lines 35-55, and col 4, lines 41-43 and reference claim 16.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to administer galactomannan with an oncolytic chemotherapeutic in order to reduce side effects produced by the chemotherapeutic agent with a reasonable expectation of success. As noted above, the reference is silent regarding "enhanced efficacy." However, the same patient population would be treated, regardless of whether the intent was to reduce side effects or enhance efficacy. Recognition of another advantage that would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. In the absence of unexpected results, it would be within the scope of the artisan to determine the optimum mode of administration and protocol regarding the relative timing of administration of the components through routine experimentation. It

would be further obvious to combine the galactomannan/chemotherapeutic treatment with other common treatments such as radiation or surgical.

A declaration signed by Yan Chang has been submitted under 37 CFR 1.131, and it is noted that the instant application has been granted 1.47 status. A declaration submitted under 37 CFR 1.131 may be signed by the following parties:

(A) All the inventors of the subject matter claimed.

(B) An affidavit or declaration by less than all named inventors of an application is accepted where it is shown that less than all named inventors of an application invented the subject matter of the claim or claims under rejection. For example, one of two joint inventors is accepted where it is shown that one of the joint inventors is the sole inventor of the claim or claims under rejection.

(C) If a petition under 37 CFR 1.47 was granted or the application was accepted under 37 CFR 1.42 or 1.43, the affidavit or declaration may be signed by the 37 CFR 1.47 applicant or the legal representative, where appropriate.

(D) The assignee or other party in interest when it is not possible to produce the affidavit or declaration of the inventor. Ex parte Foster, 1903 C.D. 213, 105 O.G. 261 (Comm'r Pat. 1903).

In this case, "(C)" applies, and Dr. Chang does not appear to be a party to the 1.47 petition. Therefore the 1.47 applicant is the assignee. The currently submitted declaration is therefore defective and has not been considered.

Claims 1-5, 7-9, 15-17, 20-23, 25, 26 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Green et al (Anti-Cancer Drug Design, 1999) and Nangia-Makker et al (Am. J. Pathol., 2000).

Green teaches that glycoamines enhance the efficacy of taxol as an apoptotic agent in an *in vitro* system. See page 160. These glycoamines are antimetastatic agents whose activity is derived from their ability to bind β–galactoside-specific lectins (galectins). See page 159 at the 1st full paragraph. The reference does not teach a galectin-binding carbohydrate comprising a polymeric carbohydrate.

Nangia-Makker teaches that galectin-3 play an essential role in tumor growth and metastasis. Furthermore, endothelial cell morphogenesis—necessary for angiogenesis—is neutralized by specific sugars. See abstract. This neutralization is due to the binding of these sugars to galectin. One binding entity exemplified is modified citrus pectin. See page 903 and page 907, 1st full paragraph. This agent completely inhibits cell motility and organization in capillary tube formation. In discussing this reference, Applicant admits that it teaches "[t]he materials of the present invention have been demonstrated to interact with galectins and inhibit angiogenesis." See specification at page 11, lines 15-20.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Green by the substitution of another agent, such as modified citrus pectin, demonstrated to have ability to bind galectin and interfere with processes necessary for tumor progression with a reasonable expectation of success. Green had taught the combination of a galactin-binding carbohydrate product increases the efficacy of a chemotherapeutic agent in the treatment of cancer, and Nangia-Makker had taught that modified

citrus pectin binds galectin and inhibits metastasis and angiogenesis, important in treating cancer. It would be within the scope of the artisan to optimize the timing of the administration of the two agents through routine experimentation.

Applicant cites a number of declarations demonstrating that the combination of a modified pectin and a chemotherapeutic results in an increase in efficacy of the chemotherapeutic. Applicant argues that this effect would not be seen if modified pectin were simply an anti-metastatic agent. However, it was known at the time of the invention and admitted by Applicant that modified citrus pectin has anti-angiogenic activity as well as anti-metastatic activity. Furthermore, Green has demonstrated increased efficacy, and suggests the possibility of synergism, of a chemotherapeutic by the addition of a galectin-binding agent. Therefore, these reported results would not be considered to be unexpected.

It is noted that the Han declaration demonstrates some synergism under very limited circumstances—the use of one particular polymeric carbohydrate and one particular chemotherapeutic with a particular protocol requiring a 48 hour incubation of the cells used in the *in vitro* assay used. Even if this limited showing of synergism were enough to overcome the prima facie case, said showing is not remotely commensurate in scope with the claims.

Claims 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Green et al (Anti-Cancer Drug Design, 1999) and Nangia-Makker et al (Am. J. Pathol., 2000) as applied to claims -5, 7-9, 15-17, 20-23, 25, 26 and 28 above, and further in view of Raz et al (US 5,834,442).

Green and Nangia-Makker teach as set forth above. The references are silent regarding particular routes of administration.

Raz teaches that oral and intravenous administration of modified citrus pectin in the treatment of cancer is known. See col 2, lines 4-33.

It would have been obvious to one having ordinary skill in the art to modify the method of Green as set forth above. It would be further within the scope of the artisan to select any routine route of administration, such as oral or intravenous. One of ordinary skill would reasonably expect success in using either of these routes because they had been disclosed by Raz as being useful for administering modified citrus pectin.

Claims 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Green et al (Anti-Cancer Drug Design, 1999) and Nangia-Makker et al (Am. J. Pathol., 2000) as applied to claims -5, 7-9, 15-17, 20-23, 25, 26 and 28 above, and further in view of Platt et al (WO 97/34907), Ros et al, (Carbohyd. Res., 1996) and Renard et al, (Carbohyd. Res., 1995).

Platt teaches that modified citric pectin (MCP) with molecular weight of about 10 kD has utility in the treatment and prevention of metastatic cancer. See pages 1-3 and page 6, lines 2-6. The reference further suggests the use of other methodologies for the depolymerization of pectin.

Ros teaches the enzymatic hydrolysis of pectin. See pp 272-3.

Renard teaches the thermal hydrolysis of pectin. See pp 156-7, section 2.

It would have been obvious to one having ordinary skill in the art to modify the method of Green as set forth above. It would have been further obvious to one having ordinary skill in the art at the time the invention was made to use a pectin depolymerized by any known method,

such as enzymatic or thermal hydrolysis, known in the art to depolymerize pectin to arrive at the MCP having anti-metastatic activity for use in the method made obvious, as set forth above. Platt had taught the general physical requirements and suggested the use of other methods. Therefore it would be within the scope of the artisan to use the method taught by Ros to prepare an appropriate product through routine experimentation with a reasonable expectation of success.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Thursday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Anna Jiang (571) 272-0627, may be contacted. The fax number for Group 1600, Art Unit 1623 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished application is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

/Leigh C. Maier/

Primary Examiner, Art Unit 1623

February 15, 2008